This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. ***(currently amended)*** A compound comprising:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor **having an inhibitory constant K_i of <100 nM**; and

wherein the chelator is capable of conjugating to a cytotoxic radioisotope.

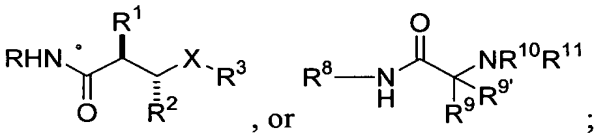
2. ***(cancelled)***

3. ***(cancelled)***

4. ***(original)*** A compound according to claim 1, comprising 1-5 targeting moieties.

5. ***(original)*** A compound according to claim 1, comprising one targeting moiety.

6. ***(currently amended)*** A compound according to claim 1, wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

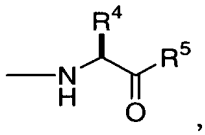


wherein,

R is independently OH or $-CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-20} alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is  , and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently **selected** at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to the linking group or a bond to the chelator; or

R^1 and R^2 taken together with the ~~nitrogen and~~ carbon ~~atom~~ **atoms** through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to ~~Ln~~ **said linking group**, a bond to ~~Ch~~ **said chelator**, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to the linking group or a bond to the chelator, provided that when R^8 is phenyl, R^{10} is ~~$-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$~~ **$-C(=O)-CHR^{12}-NH-CH(CH_3)-COOH$**;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to the linking group or a bond to the chelator;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27}, a bond to the linking group or a bond to the chelator;

or alternatively,

R^9 and R^{10} are taken together with the **nitrogen atom and** carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing ~~0-3~~ **0-2 additional** heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R^{12} is independently C_{1-20} alkyl;

R^{27} is =O, ~~C1-4 alkyl~~ C_{1-4} **alkyl**, or phenyl substituted with R^{28};

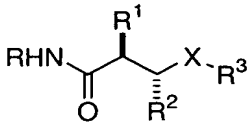
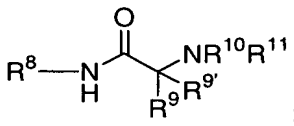
R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a ~~C5-7~~ C_{5-7} atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with ~~C1-4 alkyl~~ C_{1-4} **alkyl**.

7. ***(currently amended)*** A compound according to claim 1 ~~wherein~~

~~A compound according to claim 1~~, wherein the targeting moiety is a matrix metalloproteinase inhibitor of the formulae (Ia) or (Ib):

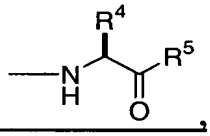


; wherein,

R is OH;

R^1 is independently selected at each occurrence from the group: H, OH, C_{1-3} alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl, and heterocycle-S-CH_2-;

R^2 is independently C_{1-6} alkyl;

X is C=O;

R^3 is  ,

R^4 is independently selected at each occurrence from the group: C_{1-6} alkyl, phenyl, and benzyl;

R^5 is independently **selected** at each occurrence from the group: NH(C_{1-6} alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to the linking group or a bond to the chelator;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula –(CH_2)$_3$-O-phenyl-CH_2-, optionally substituted with a bond to the linking group or a bond to the chelator;

or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula –(CH_2)$_3$-NH-, optionally substituted with a bond to the linking group or a bond to the chelator; or

R^1 and R^2 taken together with the ~~nitrogen and~~ carbon ~~atom~~ **atoms** through which they are attached form a C_{5-7} atom saturated ring system substituted with one

or more substituents selected from the group consisting of: a bond to ~~**Ln**~~ **said linking group**, a bond to ~~**Ch**~~ **said chelator**, and –C(=O)-$NR^{29}R^{30}$;

R^8 is OH;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the carbon atom to which R^9 and $R^{9'}$ are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O~~,~~ **and** N, ~~,~~ said ring system optionally substituted with a bond to the linking group or a bond to the chelator;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to the linking group or a bond to the chelator, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-1 heteroatoms selected from O~~,~~ **and** N, ~~,~~ said ring system optionally substituted with 0-3 R^{27}, a bond to the linking group or a bond to the chelator;

or alternatively,

R^9 and R^{10} are taken together with the **nitrogen atom and** carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing **an additional** 0-1 ~~**heteroatoms**~~ **heteroatom** selected from O~~,~~ **and** N, ~~,~~said ring system optionally substituted with a bond to the linking group or a bond to the chelator; and

R^{12} is independently C_{1-6} alkyl;

R^{27} is =O, ~~**C1-4 alkyl**~~ **C_{1-4} alkyl**, or phenyl substituted with R^{28};

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a C5-7 atom saturated ring system substituted with R^{31}; and

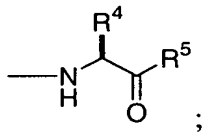
R^{31} is a benzyloxy group substituted with ~~**C1-4 alkyl**~~ **C_{1-4} alkyl**.

8. ***(currently amended)*** A compound according to claim 7 wherein:

R is –OH;

R^2 is C_{1-6} alkyl;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula $-(CH_2)_3$-O-phenyl-CH_2-;

R^5 is ~~NH(C1-6alkyl),~~ NH(C_{1-6}alkyl), substituted with a bond to the linking group or a bond to the chelator.

9. ***(currently amended)*** A compound according to claim 7, wherein:

R is –OH;

R^1 and R^2 taken together with the ~~nitrogen and~~ carbon ~~atom~~ atoms through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to ~~Ln~~ said linking group, a bond to ~~Ch~~ said chelator, and –C(=O)-$NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a ~~C5-7~~ C_{5-7} atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with ~~C1-4 alkyl~~ C_{1-4} alkyl.

10. ***(currently amended)*** A compound according to claim 1, wherein the linking group is of the formula:

$$((W^1)_h\text{-}(CR^{13}R^{14})_g)_x\text{-}(Z)_k\text{-}((CR^{13a}R^{14a})_{g'}\text{-}(W^2)_{h'})_{x'};$$

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76-84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, C_{3-10} cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, C_1-C_5 alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, ~~and~~ C_1-C_5 alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the chelator;

R^{16} is independently selected at each occurrence from the group: a bond to the chelator, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, -OPO_3H_2, -OSO_3H, aryl substituted with 0-3 R^{17}, C_{1-5} alkyl substituted with 0-1 R^{18}, C_{1-5} alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, C_{3-10} cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18}, cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to the chelator;

R^{18} is a bond to the chelator;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5; and

x' is selected from 0, 1, 2, 3, 4, and 5.

11. ***(currently amended)*** A compound according to claim 10 wherein

W^1 and W^2 are independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, $-(CH_2CH_2O)_{76-84}-$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16}, C_{3-10} cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, C_1-C_5 alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, ~~and~~ C_1-C_5 alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to the chelator;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5; and

t is selected from 0, 1, 2, 3, 4, and 5.

12. ***(original)*** A compound according to claim 10, wherein:

W^1 is C(=O)NR^{15};

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g'is 0;

h' is 1;

W^2 is NH; and

x' is 1.

13. ***(original)*** A compound according to claim 10, wherein:

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

14. ***(original)*** A compound according to claim 10, wherein:

W^1 is C(=O)NR^{15};

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or $C_{1\text{-}5}$ alkyl substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and

x' is 2.

15. ***(original)*** A compound according to claim 10, wherein:

W^1 is C(=O)NH;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

x is 1;

W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76\text{-}84}$-;

h' is 2; and

x' is 1.

16. ***(original)*** A compound according to claim 10, wherein:

x is 0;

k is 0;

g' is 3;

h' is 1;

W^2 is NH; and

x' is 1.

17. ***(currently amended)*** A compound according to claim 10, wherein:

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

R^{13a} **and** R^{14a} are independently H;

W^2 is NHC(=O) or ~~–(OCH2CH2)76-84-~~ **–(OCH_2CH_2)76-84-**; and

x' is 1.

18. ***(original)*** A compound according to claim 10, wherein:

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g'is 0;

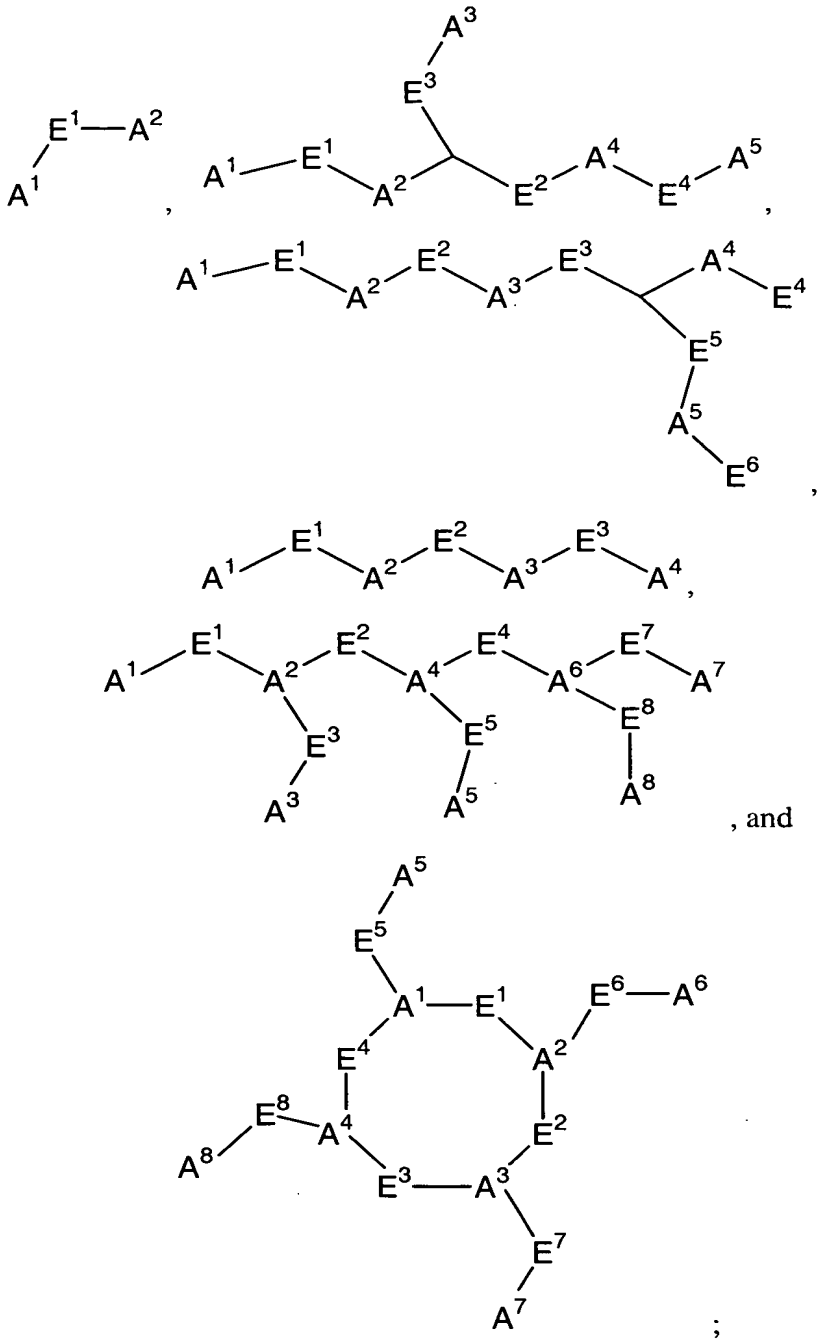
h' is 1;

W^2 is NH; and

x' is 1.

19. ***(original)*** A compound according to claim 1 wherein the linking group is absent.

20. ***(original)*** A compound according to claim 1, wherein the chelator is a metal bonding unit having a formula selected from the group:



, and

;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: N, NR^{26},NR^{19}, $NR^{19}R^{20}$, S, SH, –S(Pg), O, OH, PR^{19}, $PR^{19}R^{20}$, -O-P(O)(R^{21})-O-, $P(O)R^{21}R^{22}$, a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{16} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19} and R^{20} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{1-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{21} and R^{22} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C_1-C_{10} alkyl substituted with 0-3 R^{23}, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with

0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{23} is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, -CHO, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-SR^{24}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, NO_2, $-C(=O)NHOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_1-C_5 alkyl, C_2-C_4 alkenyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl, C_2-C_6 alkoxyalkyl, aryl substituted with 0-2 R^{24}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and

wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 or R^{23} is a bond to the linking group or targeting moiety;

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, H, C_1-C_6 alkyl, phenyl, benzyl, C_1-C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group.

21. ***(currently amended)*** A compound according to claim 20 wherein:

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: NR^{19}, $NR^{19}R^{20}$, S, SH, OH, a bond to the targeting moiety and a bond to the linking group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

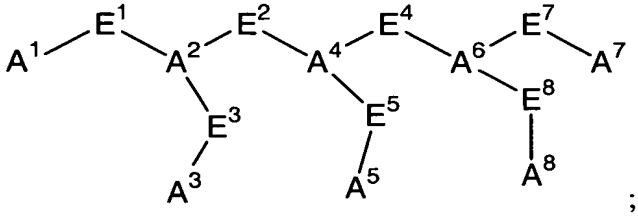
wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 and R^{23} is a bond to the linking group or a targeting moiety;

R^{19}, and R^{20} are each independently selected from the group: a bond to the targeting moiety, a bond to the linking group, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{23} is independently selected at each occurrence from the group: a bond to the targeting moiety, a bond to the linking group, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, ~~$=NOR^{18}$, $-C(=O)NHNR^{18}R^{18a}$,~~ $\underline{=NOR^{24}}$, $\underline{-C(=O)NHNR^{24}R^{24a}}$, $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, H, and C_1-C_6 alkyl.

22. ***(currently amended)*** A compound according to claim 20 wherein the chelator is of the formula:



;

A^1 is a bond to the linking group;

A^2, A^4, and A^6 are each N;

A^3, A^5, A^7 and A^8 are each OH;

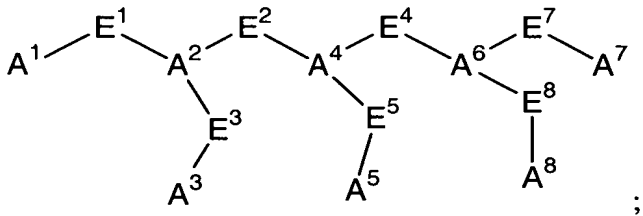
E^1, E^2, and E^4 are ~~**C2 alkyl**~~ **C_2 alkyl**;

E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23}; **and**

R^{23} is =O~~.~~.

23. ***(currently amended)*** A compound according to claim 20 wherein the chelator is of the formula:

~~**Ch**~~ **Ch** is



;

wherein:

A5 is a bond to Ln;

A^1, A^3, A^7 and A^8 are each OH;

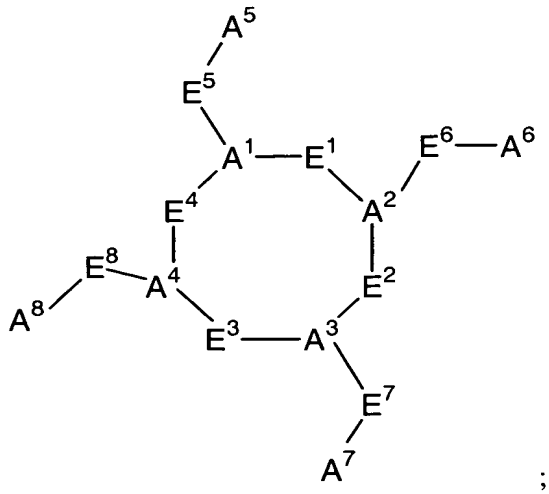
A^2, A^4 and A^6 are each NH;

E^1 , E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23};

E^2, and E^4, are C_2 alkyl;

R^{23} is =O.

24. ***(currently amended)*** A compound according to claim 20 wherein the chelator is of the formula:



;

A^1, A^2, A^3 and A^4 are each N;

A^5, A^6 and A^8 are each OH;

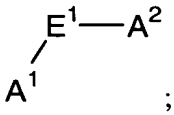
A^7 is a bond to ~~Ln~~ **said linking group**;

E^1, E^2, E^3, E^4 are each independently C_2 alkyl; and

E^5, E^6, E^7, E^8 are each independently C_2 alkyl substituted with 0-1 R^{23};

R^{23} is =O.

25. ***(original)*** A compound according to claim 20 wherein the chelator is of the formula:



;

A^1 is NR^{26};

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group;;

E^1 is a bond;

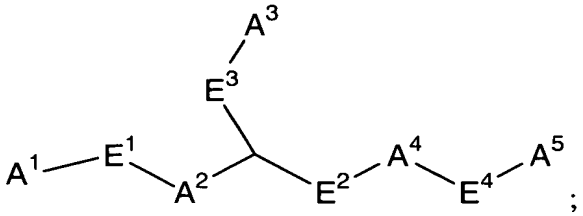
A^2 is NHR^{19};

R^{19} is a heterocycle substituted with R^{23}, the heterocycle being selected from pyridine and pyrimidine;

R^{23} is selected from a bond to the linking group, $C(=O)NHR^{24}$ and $C(=O)R^{24}$; and

R^{24} is a bond to the linking group.

26. ***(currently amended)*** A compound according to claim 20 wherein the chelator is of the formula:



;

wherein:

A^1 and A^5 are each –S(Pg);

Pg is a thiol protecting group;

E^1 and E^4 are C_2 alkyl substituted with 0-1 R^{23};

R^{23} is =O;

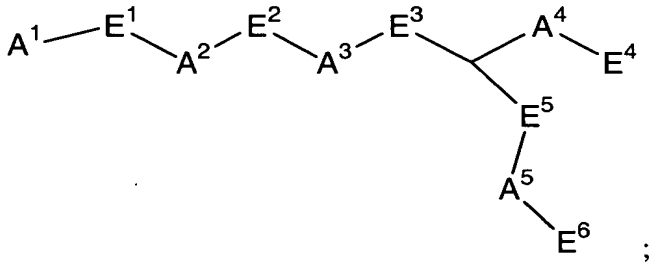
A^2 and A^4 are each –NH;

E^2 is CH_2;

E^3 is C_{1-3} alkyl substituted with 0-1 R^{23};

A^3 is a bond to ~~Ln~~ **said linking group**.

27. ***(original)*** A compound according to claim 20 wherein the chelator is of the formula:



;

wherein:

A^1 is a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2 alkyl substituted with 0-1 R^{23};

A^3 is –O-P(O)(R^{21})-O;

E^3 is C_1 alkyl;

A^4 and A^5 are each –O-;

E^4 and E^6 are each independently $C_{1\text{-}16}$ alkyl substituted with 0-1 R^{23};

E^5 is C_1 alkyl;

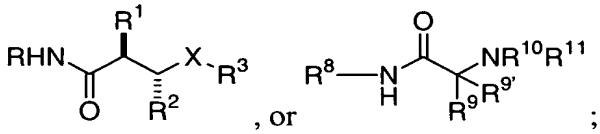
R^{21} is –OH; and

R^{23} is =O.

28. ***(currently amended)*** A compound of claim 1 having the formula:

~~$(Q)_d\text{-}L_n\text{-}C_h$~~ $(Q)_d\text{-}Ln\text{-}Ch$

wherein, **Ln is said linking group, Ch is said chelator, and** Q is a compound of Formulae (Ia) or (Ib):



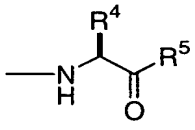
; wherein,

R is independently OH or $–CH_2SH$;

R^1 is independently selected at each occurrence from the group: H, OH, $C_{1\text{-}3}$ alkyl, $C_{2\text{-}3}$ alkenyl, $C_{2\text{-}3}$ alkynyl, and heterocycle-S-CH_2-;

R^2 is independently $C_{1\text{-}20}$ alkyl;

X is independently C=O or SO_2, provided when X is C=O, R^3 is



, and when X is SO_2, R^3 is independently selected from the group: aryl substituted with 0-2 R^6, and heterocycle substituted with 0-2 R^6;

R^4 is independently selected at each occurrence from the group: $C_{1\text{-}6}$ alkyl, phenyl, and benzyl;

R^5 is independently **selected** at each occurrence from the group: NH($C_{1\text{-}6}$ alkyl), NH-phenyl, and NH-heterocycle; wherein said alkyl, phenyl and heterocycle groups are optionally substituted with a bond to L_n;

R^6 is independently aryloxy substituted with 0-3 R^7;

R^7 is independently halogen or methoxy;

or alternatively,

R^1 and R^4 may be taken together to form a bridging group of the formula $-(CH_2)_3$-O-phenyl-CH_2-, optionally substituted with a bond to L_n;
or alternatively,

R^1 and R^2 may be taken together to form a bridging group of the formula $-(CH_2)_3$-NH-, optionally substituted with a bond to L_n; or

R^1 and R^2 taken together with the ~~nitrogen and~~ carbon ~~atom~~ **atoms** through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and $-C(=O)-NR^{29}R^{30}$;

R^8 is independently at each occurrence OH or phenyl, optionally substituted with a bond to L_n, provided that when R^8 is phenyl, R^{10} is ~~$-C(=O)-CR^{12}-NH-CH(CH_3)-COOH$~~ **$-C(=O)-CHR^{12}-NH-CH(CH_3)-COOH$**;

R^9 and $R^{9'}$ are independently H, C_{1-6} alkyl optionally substituted with a bond to L_n, or are taken together with the carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system substituted with R^6 and optionally substituted with a bond to ~~L_n~~ **Ln**;

R^{10} and R^{11} are independently H, or C_{1-6} alkyl optionally substituted with a bond to ~~L_n~~ **Ln**, or are taken together with the nitrogen atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing 0-3 heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with 0-3 R^{27} or a bond to ~~L_n~~ **Ln**;

or alternatively,

R^9 and R^{10} are taken together with the **nitrogen atom and** carbon atom to which they are attached to form a 5-7 atom saturated, partially unsaturated or aromatic ring system containing ~~0-3~~ **0-2 additional** heteroatoms selected from O, N, SO_2 and S, said ring system optionally substituted with a bond to ~~L_n~~ **Ln**;

R^{12} is independently C_{1-20} alkyl;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

~~L_n~~ **Ln** is a linking group having the formula:

$$((W^1)_h\text{-}(CR^{13}R^{14})_g)_x\text{-}(Z)_k\text{-}((CR^{13a}R^{14a})_{g'}\text{-}(W^2)_{h'})_{x'};$$

W^1 and W^2 are independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, SO_2NH, $-(OCH_2CH_2)_{76\text{-}84}$, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{16}, $C_{3\text{-}10}$ cycloalkyl substituted with 0-3 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, PO_3H, $C_1\text{-}C_5$ alkyl substituted with 0-3 R^{16}, aryl substituted with 0-3 R^{16}, benzyl substituted with 0-3 R^{16}, ~~and~~ $C_1\text{-}C_5$ alkoxy substituted with 0-3 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to ~~C_h~~ **Ch**;

R^{16} is independently selected at each occurrence from the group: a bond to C_h, $COOR^{17}$, $C(=O)NHR^{17}$, $NHC(=O)R^{17}$, OH, NHR^{17}, SO_3H, PO_3H, $-OPO_3H_2$, $-OSO_3H$, aryl substituted with 0-3 R^{17}, $C_{1\text{-}5}$ alkyl substituted with 0-1 R^{18}, $C_{1\text{-}5}$ alkoxy substituted with 0-1 R^{18}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{17};

R^{17} is independently selected at each occurrence from the group: H, alkyl substituted with 0-1 R^{18}, aryl substituted with 0-1 R^{18}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{18}, $C_{3\text{-}10}$ cycloalkyl substituted with 0-1 R^{18}, polyalkylene glycol substituted with 0-1 R^{18}, carbohydrate substituted with 0-1 R^{18},

cyclodextrin substituted with 0-1 R^{18}, amino acid substituted with 0-1 R^{18}, polycarboxyalkyl substituted with 0-1 R^{18}, polyazaalkyl substituted with 0-1 R^{18}, peptide substituted with 0-1 R^{18}, wherein the peptide is comprised of 2-10 amino acids, 3,6-O-disulfo-B-D-galactopyranosyl, bis(phosphonomethyl)glycine, and a bond to ~~C_h~~ **Ch**;

R^{18} is a bond to ~~C_h~~ **Ch**;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, and 2;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

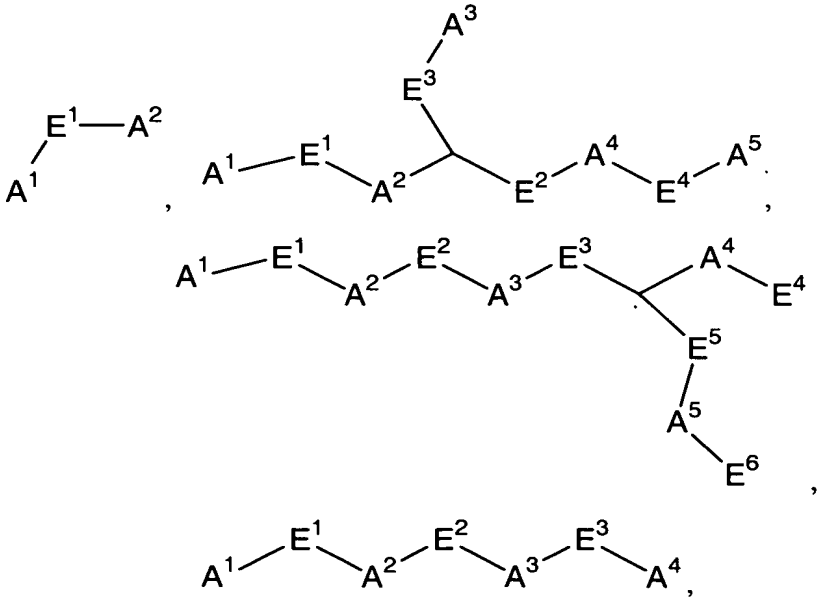
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

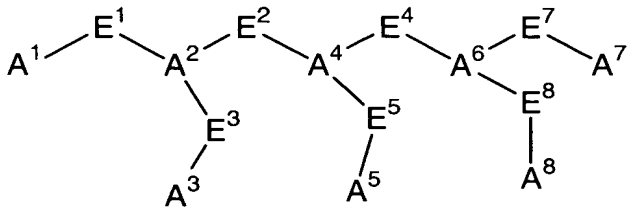
t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

x is selected from 0, 1, 2, 3, 4, and 5;

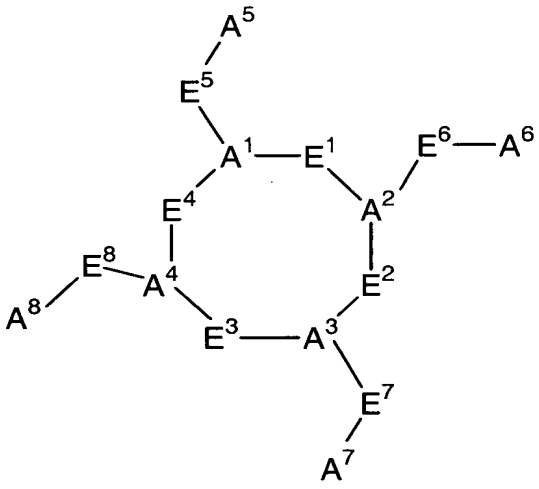
x' is selected from 0, 1, 2, 3, 4, and 5;

~~C_h~~ **Ch** is a metal bonding unit having a formula selected from the group:





, and



;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: N, NR^{26}, NR^{19}, $NR^{19}R^{20}$, S, SH, –S(Pg), O, OH, PR^{19}, $PR^{19}R^{20}$, -O-P(O)(R^{21})-O-, $P(O)R^{21}R^{22}$, a bond to the targeting moiety and a bond to the linking group;

Pg is a thiol protecting group;

E^1, E^2, E^3, E^4, E^5, E^6, E^7, and E^8 are independently a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{16} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19} and R^{20} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{1-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

R^{21} and R^{22} are each independently selected from the group: a bond to the linking group, a bond to the targeting moiety, -OH, C_1-C_{10} alkyl substituted with 0-3 R^{23}, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, heterocyclo-C_{1-10} alkyl substituted with 0-3 R^{23}, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C_{6-10} aryl-C_{1-10} alkyl substituted with 0-3 R^{23}, C_{1-10} alkyl-C_{6-10} aryl- substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{23} is independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, -CHO, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-SR^{24}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, $=NOR^{24}$, NO_2, $-C(=O)NHOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$, $-OCH_2CO_2H$, 2-(1-morpholino)ethoxy, C_1-C_5 alkyl, C_2-C_4 alkenyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl, C_2-C_6

alkoxyalkyl, aryl substituted with 0-2 R^{24}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O; and

wherein at least one of A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8 or R^{23} is a bond to the linking group or targeting moiety;

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to the linking group, a bond to the targeting moiety, H, C_1-C_6 alkyl, phenyl, benzyl, C_1-C_6 alkoxy, halide, nitro, cyano, and trifluoromethyl; and

R^{26} is a co-ordinate bond to a metal or a hydrazine protecting group; or

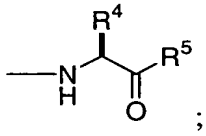
a pharmaceutically acceptable salt thereof.

29. ***(currently amended)*** A compound according to claim 28 wherein:

R is –OH;

R^2 is ~~**C1-6 alkyl**~~ **C_{1-6} alkyl**;

X is C=O;

R^3 is  ;

R^1 and R^4 are taken together to form a bridging group of formula –$(CH_2)_3$-O-phenyl-CH_2-; **and**

R^5 is ~~**NH(C1-6alkyl),**~~ **NH(C_{1-6}alkyl),** substituted with a bond to the linking group or a bond to the chelator.

30. ***(currently amended)*** A compound according to claim 28 wherein:

R is –OH;

R^9 is C_1 alkyl substituted with a bond to Ln;

R^{10} and R^{11} taken together with the nitrogen atom to which they are attached form a 5 atom saturated ring system, **wherein** said ~~**right**~~ **ring** system is substituted with 0-3 R^{27};

R^{27} is =O, ~~**C1-4 alkyl**~~ **C_{1-4} alkyl**, or phenyl substituted with R^{28}; and

R^{28} is a phenoxy group substituted with 0-2 OCH_3 groups.

31. ***(currently amended)*** A compound according to claim 28 wherein

R is –OH;

R^1 and R^2 taken together with the ~~**nitrogen and**~~ carbon ~~**atom**~~ **atoms** through which they are attached form a C_{5-7} atom saturated ring system substituted with one or more substituents selected from the group consisting of: a bond to Ln, a bond to Ch, and –C(=O)-$NR^{29}R^{30}$;

R^{29} and R^{30} taken together with the nitrogen atom through which they are attached form a ~~**C5-7**~~ **C_{5-7}** atom saturated ring system substituted with R^{31}; and

R^{31} is a benzyloxy group substituted with ~~**C1-4 alkyl**~~ **C_{1-4} alkyl**.

32. ***(currently amended)*** A compound according to claim 28 wherein

d is selected from 1, 2, 3, 4, and 5;

W^1 and W^2 are ~~**W is**~~ independently selected at each occurrence from the group: O, NH, NHC(=O), C(=O)NH, $NR^{15}C(=O)$, $C(=O)NR^{15}$, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO_2, $(OCH_2CH_2)_s$, $(CH_2CH_2O)_{s'}$, $(OCH_2CH_2CH_2)_{s''}$, $(CH_2CH_2CH_2O)_t$, and $(aa)_{t'}$;

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-1 R^{16}, C_{3-10} cycloalkyl substituted with 0-1 R^{16}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R^{16};

R^{13}, R^{13a}, R^{14}, R^{14a}, and R^{15} are independently selected at each occurrence from the group: H, =O, COOH, SO_3H, C_1-C_5 alkyl substituted with 0-1 R^{16}, aryl substituted with 0-1 R^{16}, benzyl substituted with 0-1 R^{16}, ~~**and**~~ C_1-C_5 alkoxy substituted with 0-1 R^{16}, $NHC(=O)R^{17}$, $C(=O)NHR^{17}$, $NHC(=O)NHR^{17}$, NHR^{17}, R^{17}, and a bond to ~~**Ch**~~ **Ch**;

k is 0 or 1;

s is selected from 0, 1, 2, 3, 4, and 5;

s' is selected from 0, 1, 2, 3, 4, and 5;

s" is selected from 0, 1, 2, 3, 4, and 5;

t is selected from 0, 1, 2, 3, 4, and 5;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, and A^8 are independently selected at each occurrence from the group: NR^{19}, $NR^{19}R^{20}$, S, SH, OH, and a bond to ~~L_n~~ **Ln**;

E is a bond, CH, or a spacer group independently selected at each occurrence from the group: C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, C_{3-10} cycloalkyl substituted with 0-3 R^{23}, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23};

R^{19}~~,~~ and R^{20} are each independently selected from the group: a bond to ~~L_n~~ **Ln**, hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{23}, aryl substituted with 0-3 R^{23}, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{23}, and an electron, provided that when one of R^{19} or R^{20} is an electron, then the other is also an electron;

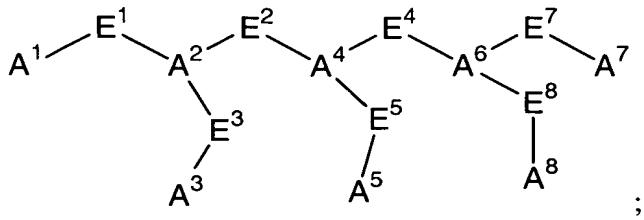
R^{23} is independently selected at each occurrence from the group: a bond to ~~L_n~~ **Ln**, =O, F, Cl, Br, I, $-CF_3$, -CN, $-CO_2R^{24}$, $-C(=O)R^{24}$, $-C(=O)N(R^{24})_2$, $-CH_2OR^{24}$, $-OC(=O)R^{24}$, $-OC(=O)OR^{24a}$, $-OR^{24}$, $-OC(=O)N(R^{24})_2$, $-NR^{25}C(=O)R^{24}$, $-NR^{25}C(=O)OR^{24a}$, $-NR^{25}C(=O)N(R^{24})_2$, $-NR^{25}SO_2N(R^{24})_2$, $-NR^{25}SO_2R^{24a}$, $-SO_3H$, $-SO_2R^{24a}$, $-S(=O)R^{24a}$, $-SO_2N(R^{24})_2$, $-N(R^{24})_2$, $-NHC(=S)NHR^{24}$, ~~$=NOR^{18}$, $-C(=O)NHNR^{18}R^{18a}$,~~ **$=NOR^{24}$, $-C(=O)NHNR^{24}R^{24a}$,** $-OCH_2CO_2H$, and 2-(1-morpholino)ethoxy; and

R^{24}, R^{24a}, and R^{25} are independently selected at each occurrence from the group: a bond to ~~L_n~~ **Ln**, H, and C_1-C_6 alkyl~~; and~~.

33. ***(currently amended)*** A compound according to claim 28 wherein

d is 1,

~~Ch~~ **Ch** is



;

A^1 is a bond to L_n;

A^2, A^4, and A^6 are each N;

A^3, A^5, A^7 and A^8 are each OH;

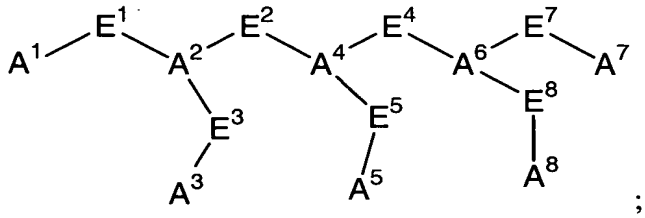
E^1, E^2, and E^4 are ~~C2 alkyl~~ **C_2 alkyl**;

E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23}; **and**

R^{23} is =O~~;~~.

34. ***(currently amended)*** A compound according to claim 28 wherein

~~Ch~~ **Ch** is



;

wherein:

~~A5~~ **A^5** is a bond to Ln;

A^1, A^3, A^7 and A^8 are each OH;

A^2, A^4 and A^6 are each NH;

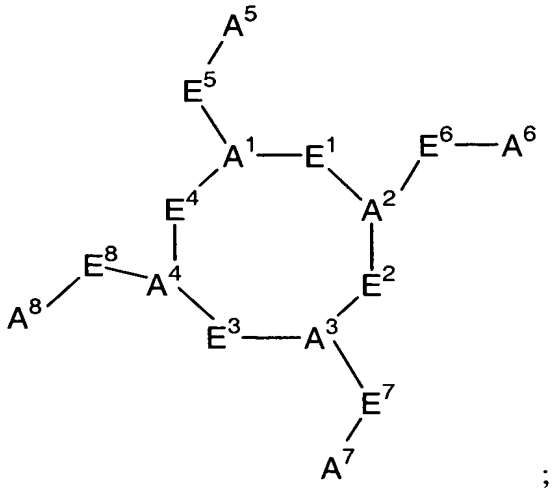
E^1, E^3, E^5, E^7, and E^8 are C_2 alkyl substituted with 0-1 R^{23};

E^2, and E^4, are C_2 alkyl;

R^{23} is =O.

35. ***(currently amended)*** A compound according to claim 28 wherein

Ch is



;

A^1, A^2, A^3 and A^4 are each N;

A^5, A^6 and A^8 are each OH;

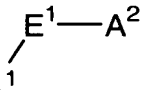
A^7 is a bond to L_n;

E^1, E^2, E^3, E^4 are each independently, C_2 alkyl; and

E^5, E^6, E^7, E^8 are each independently, C_2 alkyl substituted with 0-1 R^{23}; **and**

R^{23} is =O~~;~~.

36. ***(currently amended)*** A compound according to claim 28 wherein

~~Ch~~ **Ch** is  ;

A^1 is NR^{26};

R^{26} is a co-ordinate bond to a metal; or a hydrazine protecting group;

E^1 is a bond;

A^2 is NHR^{19};

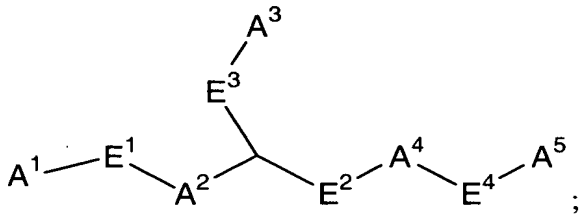
R^{19} is a heterocycle substituted with R^{23}, the heterocycle being selected from pyridine and pyrimidine;

R^{23} is selected from a bond to L_n, $C(=O)NHR^{24}$ and $C(=O)R^{24}$; and

R^{24} is a bond to ~~L_n~~ **Ln**.

37. ***(currently amended)*** A compound according to claim 28 wherein

Ch is



;

wherein:

A^1 and A^5 are each –S(Pg);

Pg is a thiol protecting group;

E^1 and E^4 are C_2 alkyl substituted with 0-1 R^{23};

R^{23} is =O;

A^2 and A^4 are each –NH;

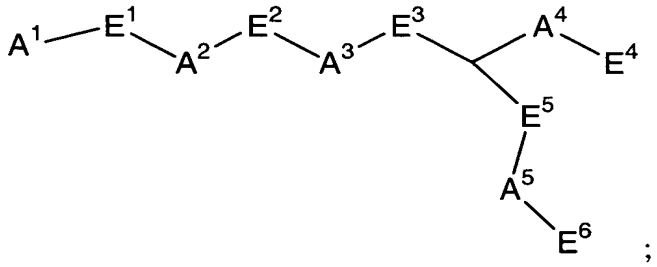
E^2 is CH_2;

E^3 is ~~**C1-3 alkyl**~~ **C_{1-3} alkyl** substituted with 0-1 R^{23};

A^3 is a bond to Ln.

38. ***(currently amended)*** A compound according to claim 28 wherein

Ch is



;

wherein:

A^1 ~~**is**~~ **is** a bond to Ln;

E^1 is C_1 alkyl substituted by R^{23};

A^2 is NH;

E^2 is C_2 alkyl ~~**sunstituted wth**~~ **substituted with** 0-1 R^{23};

A^3 is –O-P(O)(R^{21})-O;

E^3 is C_1 alkyl;

A^4 and A^5 are each –O-;

E^4 and E^6 are each independently $C_{1\text{-}16}$ alkyl substituted with 0-1R^{23};

E^5 is C_1 alkyl;

A^5 is –O-;

R^{21} is –OH; and

R^{23} is =O.

39. ***(original)*** A compound according to claim 28 wherein

W^1 is C(=O)NR^{15};

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g'is 0;

h' is 1;

W^2 is NH; and

x' is 1.

40. ***(original)*** A compound according to claim 28 wherein

x is 0;

k is 1;

Z is aryl substituted with 0-3 R^{16};

g' is 1;

W^2 is NH;

R^{13a} and R^{14a} are independently H;

h' is 1; and

x' is 1.

41. ***(currently amended)*** A compound according to claim 28 wherein

W^1 is $C(=O)NR^{15}$;

h is 1;

g is 2;

R^{13} and R^{14} are independently H;

x is 1;

k is 0;

g' is 1;

R^{13a} and R^{14a} are independently H; or ~~**C1-5 alkyl**~~ **C_{1-5} alkyl** substituted with 0-3 R^{16};

R^{16} is SO_3H;

W^2 is NHC(=O) or NH;

h' is 1; and

x' is 2.

42. ***(original)*** A compound according to claim 28 wherein

W^1 is C(=O)NH;

h is 1;

g is 3;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

x is 1;

W^2 is -NH(C=O)- or $-(OCH_2CH_2)_{76-84}-$;

h' is 2; and

x' is 1.

43. ***(original)*** A compound according to claim 28 wherein

x is 0;

k is 0;

g' is 3;

h' is 1;

W^2 is NH; and

x' is 1.

44. ***(currently amended)*** A compound according to claim 28 wherein

x is 0;

Z is aryl substituted with 0-3 R^{16};

k is 1;

g' is 1;

R^{13a} **and** R^{14a} are independently H;

W^2 is NHC(=O) or ~~–(OCH2CH2)76-84-~~ **–(OCH_2CH_2)76-84-**; and

x' is 1.

45. ***(original)*** A compound according to claim 28 wherein

W^1 is C=O;

g is 2;

R^{13} and R^{14} are independently H;

k is 0;

g' is 0;

h' is 1;

W^2 is NH; and

x' is 1.

46. ***(currently amended)*** A compound according to claim 1 selected from the group consisting of:

2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-{[5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid;

2-[7-({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

2-{7-[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl]-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl}acetic acid;

2-(7-{[N-(1-{N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}-2-sulfoethyl)carbamoyl]methyl}-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl)acetic acid;

2-[7-({N-[1-(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)-2-sulfoethyl]carbamoyl}methyl)-1,4,7,10-tetraaza-4,10-bis(carboxymethyl)cyclododecyl]acetic acid;

~~2-({2-[({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)(carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;~~

2-[({2-[({N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}acetylamino)propyl]carbamoyl}methyl)(carboxymethyl)]amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;

2-[(2-{[(N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-carbonylamino}methyl)phenyl]methyl}carbamoyl)methyl](carboxymethyl)amino}ethyl){2-[bis(carboxymethyl)amino]ethyl}amino]acetic acid;

N-[3-(2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino} acetylamino)propyl]-4,5-bis[2-(ethoxyethylthio)acetylamino]pentanamide;

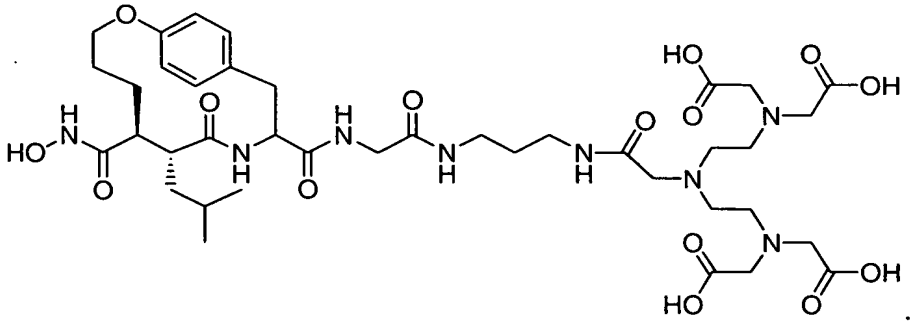
N-{[4-({[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}methyl)-phenyl]methyl}-4,5-bis[2-(ethoxyethylthio)acetylamino]-pentanamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-α,ω-dicarbonylPEG3400-2-{[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]carbonylamino}-N-(3-aminopropyl)acetamide;

1-(1,2-Dipalmitoyl-sn-glycero-3-phosphoethanolamino)-α,ω-dicarbonylPEG3400-[7-(N-hydroxycarbamoyl)(3S,6R,7S)-4-aza-6-(2-methylpropyl)-11-oxa-5-oxobicyclo[10.2.2]hexadeca-1(15),12(16),13-trien-3-yl]-N-{[4-(aminomethyl)phenyl]methyl}carboxamide conjugate;

2-[2-({5-[N-(5-(N-hydroxycarbamoyl)(5R)-5-{3-[4-(3,4-dimethoxyphenoxy)phenyl]-3-methyl-2-oxopyrrolidinyl}pentyl)carbamoyl](2-pyridyl)}amino)(1Z)-2-azavinyl]benzenesulfonic acid;

2-(2-{[5-(N-{3-[3-(N-hydroxycarbamoyl)(4S)-4-({4-[(4-methylphenyl)methoxy]piperidyl}carbonyl)piperidyl]-3-oxopropyl}carbamoyl)(2-pyridyl)]amino}(1Z)-2-azavinyl)benzenesulfonic acid; and



47. ***(original)*** A radiopharmaceutical comprising a compound of claim 1 and a cytotoxic radioisotope which is complexed to the chelator.

48. ***(original)*** A radiopharmaceutical comprising a compound of claim 28 and a cytotoxic radioisotope which is complexed to the chelator.

49. ***(original)*** A radiopharmaceutical comprising a compound of claim 46 and a cytotoxic radioisotope.

50. ***(currently amended)*** A radiopharmaceutical according to claim **49** ~~20~~ **wherein the compound is** selected from the group consisting of:

2-{[5-(3-{2-[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-acetylamino}-propylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; and

2-{[5-(4-{[(6-Hydroxycarbamoyl-7-isobutyl-8-oxo-2-oxa-9-aza-bicyclo[10.2.2]hexadeca-1(15),12(16),13-triene-10-carbonyl)-amino]-methyl}-benzylcarbamoyl)-pyridin-2-yl]-hydrazonomethyl}-benzenesulfonic acid; **and**

wherein the cytotoxic radioisotope is ^{99m}Tc.

51. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of beta particle emitters, alpha particle emitters, and Auger electron emitters.

52. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re, ^{188}Re, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{149}Pm, ^{90}Y, ^{212}Bi, ^{103}Pd, ^{109}Pd, ^{159}Gd, ^{140}La, ^{198}Au, ^{199}Au, ^{169}Yb, ^{175}Yb, ^{165}Dy, ^{166}Dy, ^{67}Cu, ^{105}Rh, ^{111}Ag, and ^{192}Ir.

53. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re, ^{188}Re, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{149}Pm, ^{90}Y, ^{212}Bi, ^{103}Pd, and ^{105}Rh.

54. ***(original)*** A radiopharmaceutical according to claim 47 wherein the cytotoxic radioisotope is selected from the group consisting of: ^{186}Re, ^{188}Re, ^{153}Sm, ^{166}Ho, ^{177}Lu, ^{149}Pm, ^{90}Y, and ^{212}Bi.

55. ***(original)*** A composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

56. ***(currently amended)*** A radiopharmaceutical composition comprising a **radiopharmaceutical** ~~**compound**~~ of claim 47, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

57. ***(original)*** A radiopharmaceutical composition **comprising**: ~~**according to claim 56, further comprising**~~

a compound comprising:

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor; and

wherein the chelator is capable of conjugating to a cytotoxic radioisotope;

a cytotoxic radioisotope which is complexed to the chelator;

a pharmaceutically acceptable carrier; and

at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

58. ***(original)*** A radiopharmaceutical composition according to claim 57, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetrorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate,

isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

59. ***(currently amended)*** A radiopharmaceutical composition according to claim 57, wherein **said** radiosensitizer agent is selected from the group **consisting** ~~consiting~~ of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholine carboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

60. ***(original)*** A kit comprising a compound of Claim 1, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

61. ***(currently amended)*** A radiopharmaceutical kit comprising a **radiopharmaceutical** ~~compound~~ of Claim 47, or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable carrier.

62. ***(original)*** A kit of Claim 60 further comprising a stabilizer.

63. ***(original)*** A radiopharmaceutical kit according to Claim 61, wherein the radioisotope is ^{186}Re or ^{188}Re and the kit further comprises one or more ancillary ligands and a reducing agent.

64. ***(original)*** A radiopharmaceutical kit according to Claim 63, wherein the ancillary ligands are tricine and a phosphine.

65. *(currently amended)* A kit **comprising:** ~~**according to claim 60, further comprising and**~~ **a compound comprising:**

i) 1-10 targeting moieties;

ii) a chelator; and

iii) 0-1 linking groups between the targeting moiety and chelator;

wherein the targeting moiety is a matrix metalloproteinase inhibitor; and

wherein the chelator is capable of conjugating to a cytotoxic radioisotope;

at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof~~,~~ **; and**

a pharmaceutically acceptable carrier.

66. *(original)* A kit according to Claim 65, wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetrorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

67. *(currently amended)* A kit according to Claim 65, wherein radiosensitizer agent is selected from the group ~~**consiting**~~ **consisting** of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-

acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

68. ***(currently amended)*** A method of treating a pathological disorder mediated by a matrix metalloproteinase in a patient which comprises ~~**administring**~~ **administering** to a patient in need thereof a therapeutically effective amount of a radiopharmaceutical according to claim 47~~,~~ and a pharmaceutically acceptable carrier.

69. ***(original)*** A method of claim 68, wherein the disorder is selected from the group consisting of atherosclerosis, restenosis, angiogenesis, tumor metastasis, tumor growth, osteoarthritis, and rheumatoid arthritis.

70. ***(currently amended)*** A method of claim 68, wherein the disorder is age related macular degeneration, diabetic retinopathy, proliferative **vitreoretinopathy, retinopathy** ~~**vitreoretinopathy,retinopathy**~~ of prematurity, ocular tumors, ocular angiogenesis/neovascularization **or** ~~**and**~~ corneal graft rejection.

71. ***(original)*** A method of claim 68, wherein the disorder is cancer selected from the group consisting of prostate, breast, colon, lung melanoma and lymph cancer.

72. ***(original)*** A method of inhibiting proliferation of cancer cells, comprising contacting the cancer cells with a proliferation-inhibitory amount of a radiopharmaceutical of claim 47.

73. ***(currently amended)*** A method of claim 68, wherein the matrix metalloproteinase is selected from the group ~~**consiting**~~ **consisting** of: MMP-1, MMP-2, MMP-3, MMP-9, and MMP-14.

74. ***(currently amended)*** A method of claim 68 wherein the matrix metalloproteinase is selected from the group ~~**consiting**~~ **consisting** of: MMP-2, MMP-9, and MMP-14.

75. ***(original)*** A method of treating cancer in a patient comprising: administering to a patient in need thereof a therapeutic radiopharmaceutical of claim 47 or a pharmaceutically acceptable salt thereof, and at least one agent selected from the group consisting of a chemotherapeutic agent and a radiosensitizer agent, or a pharmaceutically acceptable salt thereof.

76. ***(original)*** A method according to claim 75 wherein the chemotherapeutic agent is selected from the group consisting of mitomycin, tretinoin, ribomustin, gemcitabine, vincristine, etoposide, cladribine, mitobronitol, methotrexate, doxorubicin, carboquone, pentostatin, nitracrine, zinostatin, cetrorelix, letrozole, raltitrexed, daunorubicin, fadrozole, fotemustine, thymalfasin, sobuzoxane, nedaplatin, cytarabine, bicalutamide, vinorelbine, vesnarinone, aminoglutethimide, amsacrine, proglumide, elliptinium acetate, ketanserin, doxifluridine, etretinate, isotretinoin, streptozocin, nimustine, vindesine, flutamide, drogenil, butocin, carmofur, razoxane, sizofilan, carboplatin, mitolactol, tegafur, ifosfamide, prednimustine, picibanil, levamisole, teniposide, improsulfan, enocitabine, lisuride, oxymetholone, tamoxifen, progesterone, mepitiostane, epitiostanol, formestane, interferon-alpha, interferon-2 alpha, interferon-beta, interferon-gamma, colony stimulating factor-1, colony stimulating factor-2, denileukin diftitox, interleukin-2, and leutinizing hormone releasing factor.

77. ***(currently amended)*** A method according to claim 75 wherein the radiosensitizer agent is selected from the group ~~consiting~~ **consisting** of 2-(3-nitro-1,2,4-triazol-1-yl)-N-(2-methoxyethyl)acetamide, N-(3-nitro-4-quinolinyl)-4-morpholinecarboxamidine, 3-amino-1,2,4-benzotriazine-1,4-dioxide, N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide, 1-(2-nitroimidazol-1-yl)-3-(1-piperidinyl)-2-propanol, and 1-(2-nitro-1-imidazolyl)-3-(1-aziridino)-2-propanol.

78. ***(original)*** A process for the preparation of a radiopharmaceutical, said process comprising generating a macrostructure from a plurality of molecular components

wherein the plurality of components includes a compound of claim 1 and a cytotoxic radioisotope.

79. ***(canceled)***